

WHAT IS CLAIMED:

1. A method of avoiding, decreasing or overcoming the resistance of hematologic malignant cells or solid non-hematologic tumor cells to at least one chemotherapeutic agent, comprising administering an anti-cytokine antibody or
5 fragment thereof or cytokine antagonist to a patient diagnosed with a hematologic malignancy or a solid, non-hematologic tumor prior, concurrent or after administration of at least one chemotherapeutic agent.
2. The method of Claim 1, wherein said hematologic cells comprise B
10 cell lymphoma or leukemia cells.
3. The method of Claim 2, wherein said B cell lymphoma is selected from the group consisting of low grade/ follicular non-Hodgkin's lymphoma (NHL), small lymphocytic (SL) NHL, intermediate grade/ follicular NHL, intermediate grade
15 diffuse NHL, high grade immunoblastic NHL, high grade lymphoblastic NHL, high grade small non-cleaved cell NHL, bulky disease NHL and Waldenstrom's Macroglobulinemia.
4. The method of Claim 3, wherein said B cell lymphoma is low grade/
20 follicular non-Hodgkins lymphoma (NHL).
5. The method of Claim 2, wherein said leukemic cell is selected from the group consisting of acute lymphoblastic leukemia, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia, lymphoblastic
25 leukemia, lymphocytic leukemia, monocytic leukemia, myelogenous leukemia, and promyelocytic leukemia.
6. The method of Claim 1, wherein said at least one chemotherapeutic agent is selected from the group consisting of CHOP, ICE, Mitozantrone, Cytarabine,
30 DVP, ATRA, Idarubicin, hoelzer chemotherapy regime, La La chemotherapy regime,

ABVD, CEOP, 2-CdA, FLAG & IDA with or without subsequent G-CSF treatment), VAD, M & P, C-Weekly, ABCM, MOPP, DHAP, daunorubicin, doxorubicin, tamoxifen, toremifene, methotrexate, and cisplatin.

5 7. The method of Claim 1, wherein said cytokine is selected from the group consisting of IL2, IL6, IL10 and TNF-alpha.

8. The method of Claim 7, wherein said cytokine is IL10.

10 9. The method of Claim 8, wherein said anti-IL10 antibody is a humanized or human monoclonal antibody.

15 10. The method of Claim 9, wherein said anti-IL10 antibody is administered at a dosage of 0.01 to 1000 mg/kg body weight.

11. The method of Claim 10, wherein the dosage of antibody ranges from about 0.1 to 50 mg/kg of body weight.

20 12. The method of Claim 1, wherein said anti-cytokine antibody is administered concurrently with and/or prior to said chemotherapeutic agent.

13. The method of Claim 12, wherein said anti-cytokine antibody is administered concurrently or from about one hour to thirty days prior to administration of the chemotherapeutic agent.

25 14. The method of Claim 1, wherein the serum of said lymphoma patient is tested for cytokine profiles prior to administration of said anti-cytokine antibody or fragment thereof or antagonist.

15. A kit for administering the antibody or antagonist according to the method of Claim 1.

16. A kit for testing cytokine profile according to the method of Claim 14.

17. A kit for testing cytokine profile and administering antibody or antagonist according to the method of Claim 16.

18. A method of avoiding, decreasing or overcoming the resistance of hematologic malignant cells to a therapeutic agent, comprising administering an anti-cytokine antibody or cytokine antagonist to a patient diagnosed with a hematologic malignancy.

19. A method of avoiding, decreasing or overcoming the resistance of hematologic malignant cells to apoptosis induced by a therapeutic agent, comprising administering an anti-cytokine antibody or cytokine antagonist to a patient diagnosed with a hematologic malignancy.

20. The method of Claim 18, wherein said malignancy is a B cell lymphoma or leukemia.

21. The method of Claim 19, wherein said malignancy is a B cell lymphoma or leukemia.

22. A method of treating a patient with a hematologic malignancy who has relapsed following chemotherapy, comprising administering an anti-cytokine antibody or fragment thereof or cytokine antagonist to said patient.

23. A method of treating a patient having a hematologic malignancy who is refractory to chemotherapy, comprising administering an anti-cytokine antibody or fragment thereof or cytokine antagonist to said patient.

5 24. The method of Claim 21, wherein said malignancy is a B cell lymphoma or leukemia.

25. A method of treating a patient with a hematologic malignancy who has relapsed following therapy with a therapeutic antibody or fragment, comprising
10 administering an anti-cytokine antibody or fragment or cytokine antagonist to said patient.

26. The method of Claim 23, wherein said therapeutic antibody is an anti-
CD20, anti-CD19, anti-CD22, anti-CD37, anti-CD40, or anti-CD28 antibody.

15 27. The method of treating a patient with a hematologic malignancy who is refractory to therapy with a therapeutic antibody, comprising administering an anti-cytokine antibody or fragment or cytokine antagonist to said patient.

20 28. The method of Claim 25, wherein said hematologic malignancy is B cell lymphoma or leukemia.

29. A method of treating a B cell lymphoma patient comprising administering to said patient a therapeutically effective amount of a B cell depleting
25 antibody simultaneously with or consecutively with in either order an anti-cytokine antibody or fragment.

30. The method of Claim 29 wherein such B cell depleting antibody binds a B cell antigen selected from the group consisting of CD19, CD20, CD22, CD23,

CD27, CD37, CD53, CD72, CD73, CD74, CDw78, CD79a, CD79b, CD80, CD81, CD82, CD83, CDw84, CD85 and CD86.

31. The method of Claim ²⁹21 wherein said B cell depleting antibody binds
5 CD20.

32. The method of Claim 29 wherein said B cell depleting antibody binds
CD22.

33. The method of Claim 29, further comprising administration of at least
10 one chemotherapeutic agent.

34. The method of Claim 33, wherein said at least one chemotherapeutic
agent is selected from the group consisting of CHOP, ICE, Mitozantrone, Cytarabine,
15 DVP, ATRA, Idarubicin, hoelzer chemotherapy regime, La La chemotherapy regime,
ABVD, CEOP, 2-CdA, FLAG & IDA with or without subsequent G-CSF treatment),
VAD, M & P, C-Weekly, ABCM, MOPP, DHAP, daunorubicin, doxorubicin,
methotrexate, and cisplatin.

35. The method of Claim 33, wherein said anti-cytokine antibody or
20 antagonist is administered prior to said anti-CD20 antibody and said at least one
chemotherapeutic agent.

36. The method of Claim 29, wherein said anti-cytokine antibody or
25 antagonist is administered prior to said anti-CD20 antibody.

37. The method of Claim 29, wherein said cytokine is selected from the
group consisting of IL2, IL6, IL10 and TNF-alpha.

38. The method of Claim 37, wherein said cytokine is IL10.
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39. The method of Claim[✓] 29, wherein said anti-CD20 antibody is a chimeric, humanized or human anti-CD20 antibody.

5 40. The method Claim[✓] of 39, wherein said anti-CD20 antibody is a chimeric anti-CD20 antibody.

41. The method of Claim[✓] 40, where said chimeric anti-CD20 antibody is Rituximab®.

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42. The method of Claim[✓] 41, wherein said Rituximab® is administered at a dosage of 0.4 to 20 mg/kg body weight.

15 43. The method of Claim[✓] 33, wherein said at least one chemotherapeutic agent is part of a CHOP chemotherapeutic regimen.

20 44. The method of Claim[✓] 29, wherein said B cell lymphoma is selected from the group consisting of low grade/ follicular non-Hodgkin's lymphoma (NHL), small lymphocytic (SL) NHL, intermediate grade/ follicular NHL, intermediate grade diffuse NHL, high grade immunoblastic NHL, high grade lymphoblastic NHL, high grade small non-cleaved cell NHL, bulky disease NHL and Waldenstrom's Macroglobulinemia.

25 45. The method of Claim[✓] 44, wherein said B cell lymphoma is non-Hodgkin's lymphoma (NHL).

46. The method of Claim[✓] 45, wherein said B cell lymphoma is low-grade, follicular NHL.

47. The method of Claim 29, wherein the serum of said lymphoma patient is tested for cytokine profiles prior to administration of said anti-cytokine antibody or antagonist.

5 48. A kit for administering the anti-CD20 antibody and the anti-cytokine antibody or antagonist according to the method of Claim 29.

49. A kit for testing cytokine profile and administering anti-CD20 antibody and anti-cytokine antibody or antagonist according to the method of Claim 42.

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50. A method for treating a tumor having B cell involvement comprising administering to a patient in need of such treatment an effective amount of an antibody specific to a cytokine and a B cell depleting antibody which binds to an antigen expressed by B cells.

15 51. A kit for administering the anti-CD20 antibody and the anti-cytokine antibody or antagonist according to the method of Claim 50.

52. The method of Claim 50 wherein said anti-cytokine antibody binds to a cytokine selected from the group consisting of an interferon, interleukin, tumor necrosis factor, and colony stimulating factor.

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53. The method of Claim 51 wherein said anti-cytokine antibody binds to a cytokine selected from the group consisting of an interferon, interleukin, tumor necrosis factor, and colony stimulating factor.

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54. The method of Claim 50 wherein said anti-cytokine antibody specifically binds IL-10.

55. The method of Claim 51 wherein said anti-cytokine antibody specifically binds IL-10.

56. The method of Claim 50 wherein the B cell antigen is selected from the group consisting of CD19, CD20, CD22, CD23, CD27, CD37, CD53, CD72, CD73, CD74, CD ω 78, CD79a, CD79b, CD80, CD81, CD82, CD83, CDw84, CD85 and CD86.

57. A kit for administering the anti-CD20 antibody and the anti-cytokine antibody or antagonist according to the method of Claim 51.

58. The method of Claim 56 wherein said B cell antigen is CD20.

59. The method of Claim 58 wherein the anti-CD20 antibody is a human, humanized or chimeric anti-CD20 antibody.

60. The method of Claim 59 wherein said antibody possesses ADCC and/or CDC activity.

61. The method of Claim 59 wherein said anti-CD20 induces apoptosis of B cells.

62. The method of Claim 59 wherein said anti-CD20 antibody is Rituxan®, a chimeric anti-CD20 antibody produced by ATCC 69119.

63. The method of Claim 51 wherein said patient comprises a solid non-lymphoid tumor associated with a cancer selected from the group consisting of liver cancer, head and neck cancer, breast cancer, prostate cancer, testicular cancer, ovarian cancer, lung cancer, esophageal cancer, tracheal cancer, kidney cancer, bladder cancer, and colorectal cancer.

64. The method of Claim 50 wherein said B cell lymphoma is selected from the group consisting of low grade/ follicular non-Hodgkin's lymphoma (NHL), small lymphocytic (SL) NHL, intermediate grade/ follicular NHL, intermediate grade diffuse NHL, high grade immunoblastic NHL, high grade lymphoblastic NHL, high grade small non-cleaved cell NHL, bulky disease NHL and Waldenstrom's Macroglobulinemia.

65. The method of Claim 50 wherein said antibodies are administered by intravenous, intramuscular, intratumoral or intraperitoneal administration.

66. The method of Claim 51 wherein said antibodies are administered by intravenous, intramuscular, intratumoral or intraperitoneal administration.

67. The method of Claim 51 when said solid tumor comprises a precancer, early stage (Stage I or II solid cancer), advanced cancer (after Stage II cancer) or metastasized cancer.

68. The method of Claim 51 wherein said patient has colorectal cancer or lung cancer.

69. A method of treating colorectal cancer or lung cancer having B cell involvement comprising administering to a patient in need of such treatment an effective amount of an antibody specific to IL-10 and a depleting anti-CD20 antibody.

70. The method of Claim 69 wherein said depleting anti-CD20 antibody is a human, humanized or chimeric antibody.

71. The method of Claim 70 wherein said antibody is Rituxan® produced by ATCC 69119.

72. A method of treating B cell lymphoma in a patient in need of such treatment which treatment includes the administration of an anti-IL10 antibody.

73. A method of treating non-Hodgkin's lymphoma in a patient in need of such treatment which method comprises the administration of at least one anti-IL10 antibody.

74. A method of treating B cell lymphoma in a patient in need of such treatment which method includes the administration of anti-IL10 antibody and at least one B cell depleting antibody.

75. The method of Claim 63 wherein said B cell depleting antibody binds to a B cell antigen from the group consisting of CD19, CD20, CD22, CD23, CD27, CD37, CD53, CD72, CD73, CD74, CDw78, CD79a, CD79b, CD80, CD81, CD82, CD83, CDw84, CD85 and CD86.

76. A method of treating B cell lymphoma in a patient in need of such treatment which method comprises the administration of an anti-IL10 antibody and a B cell depleting anti-CD20 or anti-CD22 antibody.

77. A method of treating B cell lymphoma in a patient in need of such treatment comprising the administration of an anti-IL10 antibody and a B cell depleting anti-CD20 antibody.

78. A method of treating non-Hodgkin's lymphoma in a patient in need of such treatment comprising the administration of an anti-IL10 antibody and a B cell depleting antibody.

79. A method of treating non-Hodgkin's lymphoma in a patient in need of such treatment comprising the administration of an anti-IL10 antibody and a B cell depleting anti-CD20 antibody.

5 80. A method of treating non-Hodgkin's lymphoma in a patient in need of such treatment comprising the administration of an anti-IL10 antibody and a B cell depleting anti-CD22 antibody.

10 *amb B117* 81. The method of Claim 79 wherein said antibody is Rituxan®.
82. The method of Claim 79 wherein said antibody is Rituxan®.

83. A combination therapy for treating B cell lymphoma in a patient comprising the administration of a therapeutically effective amount of an anti-IL10
15 antibody, a B cell depleting anti-CD20 antibody and chemotherapy.

amb B127 84. The method of Claim 83 wherein said anti CD20 antibody is Rituxan®.

20 85. The method of Claim 83 wherein said patient has relapsed following previous treatment with a B cell depleting antibody.

amb B137 86. The method of Claim 85 wherein said antibody is Rituxan®.

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